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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,748	01/29/2001	Hisashi Narimatsu	1241.17	4282

7590 06/26/2006

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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,748	NARIMATSU ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4-18,24 and 51-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2, 4-18, 24, 51-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 2, 4-18, 24, 51-53 are currently pending in this application.

Applicants' amendments and arguments filed on 4-7-06, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 and claims 5-11, 52 which depend therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4(h) recites the phrase "a complement". It is not clear to the Examiner whether applicants contemplate a full length complement which or a fragment. Examiner requests clarification.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 6 is rejected because the invention appears to employ novel vectors. Since the vectors are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed plasmids'

sequences are not fully disclosed, nor have all the sequences required for their construction been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the plasmids. The specification does not disclose a repeatable process to obtain the vectors and it is not apparent if the DNA sequences are readily available to the public. Accordingly, it is deemed that a deposit of these plasmids should have been made in accordance with 37 CFR 1.801-1.809.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;

2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and

4. the deposit will be replaced if it should ever become inviable.

In response to the previous Office action, applicants reiterate that they have provided a signed declaration for the deposit of the plasmid pBS-hFT9(S2) in the response filed on 6-3-03 and that the plasmid pAMo-mFT9 is well-known in the art and readily reproducible by the skilled artisan (See, e.g., J. B. C., 268, 22782 (1993) and U.S. Patent No. 5,384,249 at column 30 et seq., which corresponds to Japanese laid-open Patent). Examiner respectfully disagrees.

While applicants did mention in their "remarks" that they have enclosed a signed declaration for the plasmid pBS-hFT9(S2), in reality, Examiner has now realized, that no such declaration was filed. Furthermore, Examiner respectfully disagrees with the argument that information regarding the plasmid pAMo-mFT9 is well known in the art or that it is readily reproducible by those skilled in the art, because the construction of the plasmid is described in the US Patent No. 5,384,249 and the research article in J. B. C., 268, 22782 (1993). A perusal of the patent as well as the published research paper does not make it clear that the plasmid is available to anyone commercially. Both the above documents refer back to other publications for construction or the source of original plasmid. In particular, the JBC research paper advises the reader that the construction of the plasmid pAMo will be reported elsewhere (see page 22783, column one , paragraph 3 and the foot note). References referring back to the source of the plasmid cannot be considered as equivalent to public availability. Therefore, Examiner maintains the above rejection and requests applicants provide a Declaration of deposit for all the plasmids claimed.

Claims 2, 4, and claims 5-18, 24, 51-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an enzyme with SEQ ID NO:1 or 2 having the activity of transferring fucose to an N-acetylglucosamine structure in an N-acetyllactosamine structure existing in a nonreducing terminus of a sugar chain via an alpha 1,3-linkage, but not having a similar activity to transfer fucose to N-acetylglucosamine residue in an alpha 2,3-sialyl N-acetyllactosamine structure, and the encoding polynucleotide with SEQ ID NO:3, 4, or 5, their respective full length complements, vectors comprising said polynucleotides and isolated host cells transformed with said vectors and a method of making the polypeptide

using said transformed host cells does not reasonably provide enablement for all such enzymes isolated from any source or such enzymes in which one or more amino acids are deleted (i.e., amino acids 1-55 deleted), substituted or added comprising variants, mutants and recombinants and polynucleotides encoding the same (i.e., polynucleotides comprising 280-1194 or 115-1194 of SEQ ID NO:3 or fragments of complementary sequences with no obvious function), vectors and transgenic non-human animals or plants cells transformed with said vectors and a method of making the polypeptide from such transgenic plants or animals. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 2, 4, and claims 5-18, 24, 51-53 are so broad as to encompass any alpha 1,3-fucosyltransferase isolated from any source including variants, mutants and recombinants that selectively fucosylates N-acetylglucosamine via alpha 1,3-linkage and transgenic non-human animals or plants transformed with said vectors and a method of making the polypeptide from such transgenic plants or animals. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of such enzymes broadly encompassed by the claims and the complex procedures of generating

transgenic plants and animals. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single human alpha 1,3-fucosyltransferase and generation of transformed microorganisms as opposed to generating transgenic animals. The only support regarding any genetics of animals or plants involves generating knockout animals which is exactly opposite of generating transgenics. Applicants provide no examples of a transgenic plant or animal which was generated by transfecting the claimed polynucleotides and show the production of the polypeptide from such transgenics.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. Furthermore, it is well known in the art that generating transgenic plants and animals are highly complex and all such generated transgenics may not become successful.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any alpha 1,3-fucosyltransfaase that exhibits the selective property described above because the specification does not establish: (A) regions of the protein structure which may be modified without effecting such activity; (B) the general tolerance of such alpha 1,3-fucosyltransferases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any alpha 1,3-fucosyltransferase residues with an expectation of obtaining the desired biological function; D) procedures for generating transgenic plants and animals using the claimed polynucleotide and a demonstration of the production of polypeptides from such transgenics; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any or all such alpha 1,3,-fucosyltransferase or such enzymes with an enormous number of amino acid modifications and furthermore generation of transgenic plants and animals using said polynucleotides. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of alpha 1,3-fucosyltransferases and polynucleotides encoding the same as well as making transgenics having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 2, 4-18, 24, 51-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 2, 4-18, 24, 51-53 are directed to polypeptides having the activity of transferring fucose to an N-acetylglucosamine structure in an N-acetyllactosamine structure existing in a nonreducing terminus of a sugar chain via an alpha 1,3-linkage, but not having a similar activity to transfer fucose to N-acetylglucosamine residue in an alpha 2,3-sialyl N-acetyllactosamine structure, polynucleotide encoding the same. Claims 2, 4, and claims 5-18, 24, 51-53 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides derived from SEQ ID NO:1 or 2 including modified polypeptide sequences, modified by at least one of deletion (deletion of amino acids 1-55), and polynucleotides encoding the same, that have not been disclosed in the specification. No description has been provided of all the polypeptide/polynucleotide sequences encompassed by the claims. No information, beyond the characterization of SEQ ID NO:1, 2 and 3-5 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides and the polynucleotides encoding the same. The specification does not contain any disclosure of the function of all the polypeptide sequences derived from SEQ ID NO:1 or 2, including fragments and variants within the scope of the claimed genus or the structure of polynucleotides encoding the same. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of functions. Therefore many functionally unrelated polypeptides and the polynucleotides encoding the same are encompassed within the scope of these claims. The

specification discloses only two species of the claimed genus of polypeptides and the polynucleotides encoding the same, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the both the above rejections applicants argue that claim 2 explicitly relates to SEQ ID NOS: 1 and 2, and the rejection is without basis in fact. As to claim 4, subpart (h), such recites stringent hybridization conditions, (i) which is acknowledged by the Federal Circuit as being an acceptable way of describing DNA as required by 35 U.S.C. 112, second paragraph and (ii) is acknowledged as well as enabling those of ordinary skill (Enzo Biochem, Inc. v. Gen-probe, Inc. 323 F.3d. 956 (Fed. Cir. 2002)) as required by 35 U.S.C. 112, first paragraph (See also, e.g., Example 9 of the Examiner's Training Manual on written description, discussing that a disclosed cDNA encoding a protein of known structure adequately describes isolated nucleic acids that specifically hybridize to the complement under stringent conditions. Applicants argue nonetheless, subpart (h) has been amended in order to specify the complement of the noted DNA sequences, as kindly suggested by the Examiner. As to claim 4, subparts (a)-(g), the Examiner's concerns are all mooted by the above-discussed amendments. Examiner respectfully disagrees. Contrary to applicant's argument claims 2 is not simply drawn to full length sequences. Claim 2 and claim 4 are drawn to polypeptides and

polynucleotides whose function has not been reiterated. Therefore, these claims continue to suffer from enablement and written description issues. Furthermore while applicant has amended claim 4 (part h), the amendment does to remedy the issue raised by the Examiner because of the phrase "a complement" which again suffers from written description and enablement problems. Examiner suggests applicants amend the phrase in part h to recite "the complement" or a full length complement" in order to address the issues raised above. On similar lines reiterating the function of the polypeptide in claim 2 would overcome both the written description and enablement issues raised with respect to those claims.

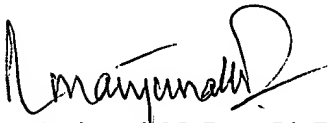
Applicants have never addressed the issue of making transgenics. A perusal of the specification does not provide any examples for making any transgenics, either non-human animals or plants. It is very well known that there is no single universal method of making transgenics using any animal or plant as hosts. However, claims are drawn to such broad limitations of making any or all transgenics. The specification is limited to teaching methods of making "knock-outs" which is almost exactly opposite of making transgenics. For all the reasons above Examiner continues to maintain the above rejections.

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura

Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

June 22, 2006